IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

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| IN RE: DIET DRUGS (PHENTERMINE/ FENFLURAMINE/DEXFENFLURAMINE) PRODUCTS LIABILITY LITIGATION | ) | MDL NO. 1203 |
| THIS DOCUMENT RELATES TO: | ) | |
| SHEILA BROWN, et al. | ) | CIVIL ACTION NO. 99-20593 |
| v. | ) | |
| AMERICAN HOME PRODUCTS CORPORATION | ) | 2:16 MD 1203 |

**MEMORANDUM IN SUPPORT OF SEPARATE PRETRIAL ORDER NO. 9402**

Bartle, J. March 17, 2015

The Estate of Jennifer E. Grundner ("Estate"), a representative claimant under the Diet Drug Nationwide Class Action Settlement Agreement ("Settlement Agreement") with Wyeth,[1] seeks benefits from the AHP Settlement Trust ("Trust"). Based on the record developed in the show cause process, we must determine whether the Estate has demonstrated a reasonable medical basis to support its claim for Matrix Compensation Benefits ("Matrix Benefits").[2]

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1. Prior to March 11, 2002, Wyeth was known as American Home Products Corporation. In 2009, Pfizer, Inc. acquired Wyeth.

2. Matrix Benefits are paid according to two benefit matrices (Matrix "A" and Matrix "B"), which generally classify Diet Drug Recipients for compensation purposes based upon the severity of

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To seek Matrix Benefits, a representative claimant[3] must first submit a completed Green Form to the Trust. The Green Form consists of three parts. The representative claimant completes Part I of the Green Form. Part II is completed by an attesting physician, who must answer a series of questions concerning the Diet Drug Recipient's medical conditions that correlate to the Matrix criteria set forth in the Settlement Agreement. Finally, if the representative claimant is represented by an attorney, the attorney must complete Part III.

Under the Settlement Agreement, only eligible claimants or representative claimants are entitled to Matrix Benefits. Generally, a claimant or representative claimant is considered eligible for Matrix Benefits if the Diet Drug Recipient is

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2. (...continued)
their medical conditions, their ages when they are diagnosed, and the presence of other medical conditions that also may have caused or contributed to the Diet Drug Recipient's valvular heart disease ("VHD"). See Settlement Agreement §§ IV.B.2.b. & IV.B.2.d.(1)-(2). Matrix A-1 describes the compensation available to representative claimants where the Diet Drug Recipients were diagnosed with serious VHD, they took the drugs for 61 days or longer, and they did not have any of the alternative causes of VHD that made the B matrices applicable. In contrast, Matrix B-1 outlines the compensation available to representative claimants where the Diet Drug Recipients were registered as having only mild mitral regurgitation by the close of the Screening Period, they took the drugs for 60 days or less, or they were diagnosed with conditions that would make it difficult for them to prove that their VHD was caused solely by the use of these Diet Drugs.

3. Under the Settlement Agreement, representative claimants include estates, administrators or other legal representatives, heirs, or beneficiaries. See Settlement Agreement § II.B.

diagnosed with mild or greater aortic and/or mitral regurgitation by an echocardiogram performed between the commencement of Diet Drug use and the end of the Screening Period.[4] See Settlement Agreement §§ IV.B.1.a. & I.22.

In June, 2012, Victoria E. Cruz, administratrix for the Estate, submitted a completed Green Form to the Trust signed by the attesting physician, Dean G. Karalis, M.D., F.A.C.C. Based on an echocardiogram dated September 9, 2002, Dr. Karalis attested in Part II of the Green Form that Jennifer E. Grundner ("Ms. Grundner") suffered from mild aortic regurgitation and aortic stenosis with an aortic valve area < 1.0 square centimeter by the Continuity Equation[5] and had surgery to repair or replace the aortic and/or mitral valve(s) following the use of Pondimin® and/or Redux™.[6] Based on such findings, the Estate would be

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4. The Screening Period ended on January 3, 2003 for echocardiograms performed outside of the Trust's Screening Program and on July 3, 2003 for echocardiograms performed in the Trust's Screening Program. See Settlement Agreement § I.49.

5. Under the Settlement Agreement, the presence of aortic stenosis requires the payment of reduced Matrix Benefits for a claim based on damage to the aortic valve. See Settlement Agreement § IV.B.2.d.(2)(c)i)e).

6. Dr. Karalis also attested that Ms. Grundner suffered from an abnormal left atrial dimension, a reduced ejection fraction in the range of 50% to 60%, and New York Heart Association Functional Class I symptoms. These conditions are not at issue in this claim.

entitled to Matrix B-1, Level III benefits in the amount of $158,264.[7]

In the report of Ms. Grundner's September 9, 2002 echocardiogram, the reviewing cardiologist, Thomas S. Davidson, M.D., observed that mild aortic regurgitation was seen. Dr. Davidson, however, did not specify a percentage as to the level of Ms. Grundner's aortic regurgitation. Under the definition set forth in the Settlement Agreement, mild or greater aortic regurgitation is present where the regurgitant jet height ("JH") in the parasternal long-axis view (or in the apical long-axis view, if the parasternal long-axis view is unavailable) is equal to or greater than ten percent (10%) of the left ventricular outflow tract height ("LVOTH"). See Settlement Agreement § I.22.

In September, 2012, the Trust forwarded the claim for review by Robert L. Gillespie, M.D., F.A.C.C., F.A.S.E., one of its auditing cardiologists. In the interim, the attesting physician, Dr. Karalis, again reviewed Ms. Grundner's September 9, 2002 echocardiogram. In a letter dated January 20, 2013, Dr. Karalis stated, in pertinent part, the following:

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7. Under the Settlement Agreement, a representative claimant is entitled to Level III benefits if the Diet Drug Recipient suffered from "left sided valvular heart disease requiring ... [s]urgery to repair or replace the aortic and/or mitral valve(s) following the use of Pondimin® and/or Redux™." Settlement Agreement § IV.B.2.c.(3)(a).

At claimant counsel's request, I reviewed Ms. Grundner's September 9, 2002 echocardiogram a second time. I was able to reaffirm my findings of mild aortic regurgitation. At the beginning of the study in the parasternal long axis view there is clearly mild [aortic regurgitation] seen. In fact the sonographer freezes the frame and measures the [aortic regurgitation] jet. Based on this, I would ask them to re-review the disc and focus on the very beginning of the study and look at the parasternal long axis view of the aortic valve with color flow Doppler. The time on the disc for this portion of the study is from 0.15 to 0.45.

My finding related to the September 9, 2002 echocardiogram is consistent with the claimant's medical history. Under a totality of the circumstances approach, the auditor can find ample basis for mild aortic regurgitation. In addition to her September 9, 2002 echocardiogram and before her valve surgery, the claimant had follow-up echocardiograms to monitor her aortic valve disease by her treating physicians. These echocardiograms strongly support that she was FDA positive during the relevant period prescribed by the settlement. On August 23, 2004, in a clinical setting, an echocardiogram found the claimant to have moderate aortic regurgitation. On February 2, 2005, also in a clinical setting, another echocardiogram found the claimant to again have moderate aortic regurgitation. The tapes for the two studies in 2004 and 2005 are not available and the findings are based upon the official readings by the clinicians who were following her aortic valve disease. On May 21, 2010, just prior to her aortic valve replacement surgery the claimant had another echocardiogram again which showed mild aortic regurgitation. This echocardiogram, as with her previous echocardiograms[,] was done in a clinical setting with the purpose of following her known aortic valve disease. I was able to review this study and I agree

> with the finding of mild aortic valve regurgitation. In my clinical experience, given the presence of aortic regurgitation by echocardiography in 2004, 2005 and 2010, and given the nature of valve disease, it is most probable that she would have had at least mild aortic regurgitation in 2002 as I found when I reviewed her September 9, 2002 echocardiogram. In addition the official report from that study which was also performed in a clinical setting was mild aortic valve regurgitation, in agreement with my interpretation of that study. Given the settlement standard and the totality of the circumstances, it is certainly reasonable to find mild aortic regurgitation following drug use and prior to the end of the screening period.

Dr. Karalis's January 20, 2013 letter was provided to Dr. Gillespie during the audit. After audit, Dr. Gillespie determined that there was no reasonable medical basis for the attesting physician's representation that Ms. Grundner had mild aortic regurgitation. In support of this conclusion, Dr. Gillespie explained:

> I have reviewed the findings [and] read the letter sent by the attesting physician Dr. Dean Karalis. He is correct that patients with [Ms. Grundner's] clinical history will often have mild [aortic regurgitation]. However, after again reviewing the only study available to me from 9/9/02, there was only trace [aortic regurgitation] on this study. I specifically focused on .15-.45 on disc as well as on the entire disc, and only trace [aortic regurgitation] was present.

Based on Dr. Gillespie's finding that Ms. Grundner did not have at least mild aortic regurgitation between the

commencement of Diet Drug use and the end of the Screening Program, the Trust issued a post-audit determination denying the Estate's claim. Pursuant to the Rules for the Audit of Matrix Compensation Claims ("Audit Rules"), the Estate contested this adverse determination.[8] In contest, the Estate argued that the auditing cardiologist did not follow the Audit Rules and "instead chose to substitute his own independent analysis of the pertinent screening echocardiogram study." In addition, the Estate asserted that the standard of review is not simple "disagreement" between the attesting physician and the auditing cardiologist; the auditing cardiologist failed to explain the rationale for his conclusion of a lack of a reasonable medical basis for the attesting physician's finding; and the auditing cardiologist improperly failed to consider Ms. Grundner's subsequent echocardiograms, which, according to the Estate, established a reasonable medical basis for the attesting physician's finding of mild aortic regurgitation "under the totality of circumstances standard adopted in the [Settlement Agreement]."

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8. Claims placed into audit on or before December 1, 2002 are governed by the Policies and Procedures for Audit and Disposition of Matrix Compensation Claims in Audit, as approved in Pretrial Order ("PTO") No. 2457 (May 31, 2002). Claims placed into audit after December 1, 2002 are governed by the Audit Rules, as approved in PTO No. 2807 (Mar. 26, 2003). There is no dispute that the Audit Rules contained in PTO No. 2807 apply to the Estate's claim.

Although not required to do so, the Trust forwarded the claim for a second review by the auditing cardiologist. Dr. Gillespie submitted a declaration in which he again concluded that there was no reasonable medical basis for Dr. Karalis's representation that Ms. Grundner had at least mild aortic regurgitation. Dr. Gillespie explained, in pertinent part:

> 10. Based on my review, I confirm my finding at audit that there is no reasonable medical basis to conclude that Claimant had mild aortic regurgitation. I again reviewed the September 9, 2002 echocardiogram study. I reviewed the contest materials, including Dr. Karalis' January 2013 letter which was initially provided to me at audit. Only trace aortic regurgitation is seen on the September 9, 2002 study. While Claimant developed mild aortic regurgitation in 2010, there is only trace aortic regurgitation on the September 2002 study, and there is no reasonable medical basis to conclude otherwise. In measuring aortic regurgitation on the September 9, 2002 study, claimant's expert measured the outflow track at its widest width, at approximately .30 in the study. The measurement should have been made using the narrow jet just prior to this point on the study, which is representative of the trace aortic regurgitation seen throughout the study. Only trace aortic regurgitation is present on the September 2002 study, and there is no reasonable medical basis to conclude otherwise.
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> 11. Accordingly, I affirm my findings at audit. Claimant had only trace aortic regurgitation, and there is no reasonable medical basis for the Attesting Physician's Green Form representation that Claimant had mild aortic regurgitation. Further, there is no reasonable medical basis to find that Claimant had mild aortic regurgitation prior to January 3, 2003.

The Trust then issued a final post-audit determination, again denying the Estate's claim. The Estate disputed this final determination and requested that the claim proceed to the show cause process established in the Settlement Agreement. See Settlement Agreement § VI.E.7.; PTO No. 2807, Audit Rule 18(c). The Trust then applied to the court for issuance of an Order to show cause why the claim should be paid. On March 21, 2014, we issued an Order to show cause and referred the matter to the Special Master for further proceedings. See PTO No. 9211 (Mar. 21, 2014).

Once the matter was referred to the Special Master, the Trust submitted its statement of the case and supporting documentation. The Estate then served a response upon the Special Master. The Trust submitted a reply on June 18, 2014. Under the Audit Rules, it is within the Special Master's discretion to appoint a Technical Advisor[9] to review claims after the Trust and the Estate have had the opportunity to develop the Show Cause Record. See Audit Rule 30. The Special Master assigned a Technical Advisor, Gary J. Vigilante, M.D., F.A.C.C.,

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9. A "[Technical] [A]dvisor's role is to act as a sounding board for the judge--helping the jurist to educate himself in the jargon and theory disclosed by the testimony and to think through the critical technical problems." Reilly v. United States, 863 F.2d 149, 158 (1st Cir. 1988). In a case such as this, where conflicting expert opinions exist, it is within the discretion of the court to appoint a Technical Advisor to aid it in resolving technical issues. Id.

to review the documents submitted by the Trust and the Estate and to prepare a report for the court. The Show Cause Record and Technical Advisor Report are now before the court for final determination. See id. Rule 35.

The issue presented for resolution of this claim is whether the Estate has met its burden of proving that there is a reasonable medical basis for finding that Ms. Grundner suffered from at least mild aortic regurgitation between the commencement of Diet Drug use and the end of the Screening Period. See id. Rule 24. Ultimately, if we determine that there is no reasonable medical basis for the answer in the Estate's Green Form that is at issue, we must affirm the Trust's final determination and may grant such other relief as deemed appropriate. See id. Rule 38(a). If, on the other hand, we determine that there is a reasonable medical basis for the answer, we must enter an Order directing the Trust to pay the claim in accordance with the Settlement Agreement. See id. Rule 38(b).

In support of its claim, the Estate reasserts the arguments it made during contest. The Estate also submitted a supplemental declaration from Dr. Karalis, in which he again opines that the auditing cardiologist is incorrect and that Ms. Grundner's September 9, 2002 echocardiogram reveals the presence of at least mild aortic regurgitation. Dr. Karalis stated, in pertinent part:

14. In the parasternal long axis view of the Grundner echocardiogram from September 9, 2002, an aortic regurgitant jet was detected by color flow Doppler in the clips marked from approximately 0.15 to 0.45. The echocardiographic review of aortic regurgitation necessitates assessment of a three dimensional jet with a two dimensional image. Hence the jet width that is chosen to qualitatively measure the degree of aortic regurgitation must be representative of the jet width not from a single frame but from multiple frames. There is one freeze frame where they actually measured the jet width and it was approximately 0.4 centimeters. Although they never measured the outflow track diameter in general, the average outflow track diameter width is approximately 2.0 centimeters. The measurement of 0.4 centimeters that they determined in the freeze frame would clearly put the regurgitant jet from the September 9, 2002 study clearly in the upper range of mild aortic regurgitation and not trace aortic regurgitation. For the aortic regurgitation to be quantified as only trace the aortic regurgitant jet must be less than 0.2 centimeters if one assumes a left ventricular outflow track diameter of 2.0 centimeters and the aortic regurgitant jet in the Grundner echocardiogram exceeds that width. It is also important to remember that this echocardiogram was performed in a clinical setting and the interpreting cardiologist also found the aortic regurgitation to be mild not trace. It is medically reasonable that over the period in the echocardiographic study where the aortic regurgitation jet was assessed that the general representation was that there was mild aortic valve regurgitation, and not just trace aortic valve regurgitation.

15. For the reasons set forth in this Declaration along with my statements in my January 20, 2013 Letter of Attestation, I again affirm that it is medically reasonable to find mild aortic regurgitation following

> the claimant's diet drug use and prior to the end of the screening period on January 3, 2003.

In response, the Trust argues that the Estate has not established a reasonable medical basis for Dr. Karalis's representation that Ms. Grundner had at least mild aortic regurgitation between the commencement of Diet Drug use and the end of the Screening Period. In addition, the Trust contends that the auditing cardiologist did not merely substitute his opinion for that of the auditing cardiologist and instead found no reasonable medical basis for the finding of mild aortic regurgitation. Finally, the Trust argued that Dr. Gillespie refuted the assertion that the "totality of the circumstances" supports a finding of mild aortic regurgitation.

The Technical Advisor, Dr. Vigilante, reviewed Ms. Grundner's September 9, 2002 echocardiogram and concluded that there was no reasonable medical basis for finding that Ms. Grundner had at least mild aortic regurgitation between the commencement of Diet Drug use and the end of the Screening Period. Specifically, Dr. Vigilante explained, in pertinent part:

> I reviewed the tape and DVD of the Claimant's echocardiogram of September 9, 2002. These were identical studies. The Claimant's name and date were documented. In addition, it was stated that the indication for the study was "Fen-Phen." It was stated that the Claimant's height was 67 inches and weight 280 pounds. This was a

limited quality study with the usual echocardiographic views obtained. The study was 4 minutes and 30 seconds long. The apical views were of limited value as there was not good endocardial definition of the left and right ventricles. However, the parasternal long axis view was interpretable. The Nyquist limit was set low at 56 cm per second at a depth of 17 cm. However, only mild color flow artifact was noted.

Evaluation of the aortic valve demonstrated that this was a thickened and calcified structure with obvious sclerosis. There was no significant stenosis. The parasternal long-axis view was available and completely interpretable for evaluation. I digitized the cardiac cycles in the parasternal long-axis view and measured the JH and LVOTH with electronic calipers. The LVOTH was 2.2 cm. A very thin jet of aortic regurgitation could be seen in the parasternal long-axis view even at the low Nyquist limit of 56 cm per second. The representative JH immediately below the aortic valve was 0.2 cm. Therefore, the JH/LVOTH ratio was 9% qualifying for trace aortic regurgitation. The sonographer measured a JH of 0.407 cm in the parasternal long-axis view. However, this was below the area where the measurement should occur and was not representative of the true JH. The representative JH was 0.2 cm. There was no sonographer-determined LVOTH on this study. The aortic valve could be seen in the apical five chamber view. This was a more limited view than the parasternal long-axis view. During color flow Doppler evaluation at a Nyquist limit of 53 cm per second at a depth of 18 cm, there was no convincing demonstration of aortic regurgitation in the apical view. It should be noted that the time frames of 0.15 to 0.45 documented by Dr. Karalis were used in my determination of the severity of aortic regurgitation on the study of September 9, 2002.

. . . .

> [T]here is no reasonable medical basis for the Attesting Physician's answer to Green Form Question C.3.b. That is, the echocardiogram of September 9, 2002 demonstrated trace aortic regurgitation with comments as above. An echocardiographer could not reasonably conclude that this study demonstrated mild aortic regurgitation even taking into account the issue of inter-reader variability when appropriate quantitative measurements were made of the regurgitant jet in the parasternal long-axis view.

In response to the Technical Advisor Report, the Estate argues that "the Technical Advisor chose to substitute his independent analysis of the pertinent echocardiographic studies rather than to consider whether under the entire record the Attesting Physician's findings were medically reasonable." In addition, the Estate maintains that the Technical Advisor "offers no basis for his assertion that the Attesting Physician's methodology or findings were medically unreasonable" and that the differences in the estimation of the level of aortic regurgitation between the Technical Advisor and the Attesting Physician are "minimal." Finally, the Estate asserts that the Technical Advisor failed to give deference to the reviewing cardiologist, Dr. Davidson, and failed to give any weight to the entirety of the Show Cause Record. Thus, according to the Estate, the Technical Advisor's findings represent a "classic substitution" of his opinion for those of the Attesting Physician and reviewing cardiologist.

After reviewing the entire Show Cause Record, we find the Estate's arguments are without merit. In particular, we do not agree with the Estate that the submissions of Dr. Karalis support a finding that Ms. Grundner had mild aortic regurgitation prior to the end of the Screening Period, that is, January 3, 2003 for echocardiograms performed outside of the Trust's Screening Program and July 3, 2003 for echocardiograms performed in the Trust's Screening Program.

Although Dr. Karalis identified a specific time frame on Ms. Grundner's echocardiogram that he contended demonstrated a jet width large enough to "put the regurgitant jet from the September 9, 2002 study clearly in the upper range of mild aortic regurgitation and not trace aortic regurgitation," this frame was not representative of the entire study. Upon review, Dr. Gillespie observed that the measurement to which Dr. Karalis referred "should have been made using the narrow jet just prior to this point on the study, which is representative of the trace aortic regurgitation seen throughout the study." Similarly, Dr. Vigilante determined that the measurement on which Dr. Karalis relied "was below the area where the measurement should occur and was not representative of the true JH."[10] Using

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10. Given the specific findings of the auditing cardiologist and the Technical Advisor, we reject the Estate's assertions that they (1) substituted their own opinion for that of the attesting physician, (2) failed to follow the Audit Rules, and (3) failed

(continued...)

representative jets, Dr. Gillespie and Dr. Vigilante each determined that Ms. Grundner's September 9, 2002 echocardiogram demonstrated only trace aortic regurgitation and that there was no reasonable medical basis to conclude that she had mild aortic regurgitation prior to the close of the Screening Period.[11]

We previously have held that for a reasonable medical basis to exist, a claimant or representative claimant must establish that the findings of the requisite level of regurgitation are representative of the level of regurgitation throughout the echocardiogram. See, e.g., Mem. in Supp. of PTO No. 6997, at 11; see also, e.g., In re Diet Drugs (Phentermine/Fenfluramine/Dexfenfluramine) Prods. Liab. Litig., 543 F.3d 179, 187 (3d Cir. 2008). To conclude otherwise would allow claimants who do not have the requisite level of regurgitation to receive Matrix Benefits, which would be contrary to the intent of the Settlement Agreement. See Mem. in Supp. of PTO No. 6997, at 11. Although Dr. Karalis acknowledged that "the

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10. (...continued)
to explain their rationale.

11. When considered along with the September 9, 2002 echocardiogram, we do not agree that Ms. Grundner's echocardiograms of August 25, 2004, February 2, 2005, and May 21, 2010, what the Estate refers to as the "totality of the circumstances," supports a finding that there was a reasonable medical basis for the Attesting Physician's finding of mild aortic regurgitation after Diet Drug use and before the end of the Screening Period.

jet width that is chosen to qualitatively measure the degree of aortic regurgitation must be representative of the jet width not from a single frame but from multiple frames," neither he nor the Estate makes any argument that the regurgitant jet identified by Dr. Karalis was representative of the level of aortic regurgitation shown throughout Ms. Grundner's September 9, 2002 echocardiogram.[12]

Finally, to the extent the Estate relies on interreader variability to establish a reasonable medical basis, such reliance is misplaced. The concept of inter-reader variability is already encompassed in the reasonable medical basis standard applicable to claims under the Settlement Agreement. Here, the auditing cardiologist and Technical Advisor concluded that Ms. Grundner's aortic regurgitation was trace.[13] Dr. Vigilante also specifically found that Ms. Grundner's largest representative JH/LVOTH ratio was 9%. Adopting the Estate's

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12. For this reason as well, we do not agree with the Estate that deference should be given to the attesting physician's findings or the findings of a reviewing cardiologist. Accepting the Estate's assertion would be inconsistent with our decision to impose a 100% audit requirement for all claims for Matrix Benefits. See Mem. in Supp. of PTO No. 2662, at 13 (Nov. 16, 2002).

13. Dr. Vigilante specifically determined that an echocardiographer could not reasonably conclude that Ms. Grundner had mild aortic regurgitation, "even taking into account the issue of inter-reader variability when appropriate quantitative measurements were made of the regurgitant jet in the parasternal long-axis view."

argument would allow a claimant or representative claimant to recover Matrix Benefits when the Diet Drug Recipient's level of aortic regurgitation is below the threshold established by the Settlement Agreement. This result would render meaningless the standards established in the Settlement Agreement.

As the Estate has not established a reasonable medical basis for finding that Ms. Grundner had at least mild aortic regurgitation between the commencement of Diet Drug use and the end of the Screening Period, the Estate's claim must be denied. Therefore, we will affirm the Trust's denial of the Estate's claim for Matrix B-1, Level III benefits.